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10/672,067	09/29/2003	Lawrence C. Paoletti	7570/80639	4716

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LAW OFFICE OF MICHAEL A. SANZO, LLC
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ROCKVILLE, MD 20855

EXAMINER

BEISNER, WILLIAM H

ART UNIT	PAPER NUMBER
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1744

MAIL DATE	DELIVERY MODE
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07/11/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/672,067

Applicant(s)

PAOLETTI ET AL.

Examiner

William H. Beisner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18,21-25,30-37 and 39-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18,21-25,30-37 and 39-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 18, 21-25, 30-37 and 39-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Besnainon et al.(US 5,064,764).

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The reference of Besnainon et al. discloses a culture apparatus that is structurally the same as that instantly claimed. Specifically the reference discloses a fermentor (18) with an inlet port (22) and an outlet port (38). The device includes a culture vessel (14) with an inlet port (16 or 32) which is connected to outlet port (38) of the fermentor (18) and an outlet port (40). The device includes a means (36) for moving fluid from the outlet port (38) of the fermentor (18) to the inlet port (16 or 32) of the culture vessel (14) and means (46) for removing fluid from the outlet port (40) of the culture vessel (14).

With respect to claims 18 and 39, while the reference of Besnainon et al. discloses that the fermentor (18) includes a second outlet port (24) that is not connected to the culture vessel (14), the reference does not specifically disclose a means for moving fluid out of the fermentor and through the second port (24).

The reference of Besnainon et al. discloses that the second port (24) is for taking samples and is connected to an analyzer device (See column 4, lines 18-26). The use of pumps and/or valves for controlling the flow of a fluid through a conduit is known in the art as evidenced by pumps (30 and 36) in the system of Besnainon et al.

In view of this disclosure, it would have been obvious to one of ordinary skill in the art to provide the outlet (24) of the system of Besnainon et al. with a pump device for the known and expected result of providing an art recognized means for controlling the flow of sample from the fermentor.

With respect to the recited solid support of claims 18 and 39, the culture vessel of Besnainon et al. includes a membrane material that is capable of supporting attached cells. Additionally, the instant claim language fails to positively recite the solid support as part of the

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claimed device. The instant claim language merely recites “a culture vessel for growing eukaryotic cells attached to a solid support”. The claim never positively recites that the culture vessel includes or comprises a solid support.

With respect to claims 21 and 40, the reference discloses reservoir (26) connected to an inlet port on the fermentor (See Figure 1) and a means (30) for removing medium from the reservoir to the inlet port of the fermentor.

With respect to claims 22, 23, 41 and 42, while the reference discloses only a single reservoir, inlet port and pump, the reference discloses that it is desirable to add glucose, glutamine or amino acids to the fermentor (See column 4, lines 23-26).

In the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to provide the system with individual vessels of glucose, glutamine and amino acids for the known and expected results of providing a means recognized in the art for allowing the control of the individual components of the medium added to the fermentor vessel.

With respect to claim 24, since the solid support has not been positively recited as part of the claimed structure, claim 24 does not further structurally define or limit the device of claim 18.

With respect to claims 25, elements (36) and (46) are pumps.

With respect to claims 30-35, the reference discloses the use of pumps (30, 36, 46) for controlling the flow of fluid within the culture system.

With respect to claims 36 and 37, the fermentor (18) includes a motor driven mixing paddle (20).

5. Claims 18, 21-23, 25, 30-37 and 39-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Besnainon et al.(US 5,064,764) in view of Tolbert et al. (US 4,537,860).

The reference of Besnainon et al. discloses a culture apparatus that is structurally the same as that instantly claimed. Specifically the reference discloses a fermentor (18) with an inlet port (22) and an outlet port (38). The device includes a culture vessel (14) with an inlet port (16 or 32) which is connected to outlet port (38) of the fermentor (18) and an outlet port (40). The device includes a means (36) for moving fluid from the outlet port (38) of the fermentor (18) to the inlet port (16 or 32) of the culture vessel (14) and means (46) for removing fluid from the outlet port (40) of the culture vessel (14).

With respect to claims 18 and 39, while the reference of Besnainon et al. discloses that the fermentor (18) includes a second outlet port (24) that is not connected to the culture vessel (14), the reference does not specifically disclose a means for moving fluid out of the fermentor and through the second port (24).

The reference of Besnainon et al. discloses that the second port (24) is for taking samples and is connected to an analyzer device (See column 4, lines 18-26). The use of pumps and/or valves for controlling the flow of a fluid through a conduit is known in the art as evidenced by pumps (30 and 36) in the system of Besnainon et al.

In view of this disclosure, it would have been obvious to one of ordinary skill in the art to provide the outlet (24) of the system of Besnainon et al. with a pump device for the known and expected result of providing an art recognized means for controlling the flow of sample from the fermentor.

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Claims 18 and 39 differ by reciting that the device is intended to be used with a solid support for cell attachment.

The reference of Tolbert et al. discloses that a bioreactor that is similar in structure and function to that of the primary reference can be used to culture free cells or attached cells to bead carriers (See column 7, lines 40-60).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to provide the bioreactor of the primary reference with carrier beads for the known and expected result of allowing adhering cells to be cultured within the system of the primary reference as is conventional in the art.

With respect to claims 21 and 40, the reference discloses reservoir (26) connected to an inlet port on the fermentor (See Figure 1) and a means (30) for removing medium from the reservoir to the inlet port of the fermentor.

With respect to claims 22, 23, 41 and 42, while the reference discloses only a single reservoir, inlet port and pump, the reference discloses that it is desirable to add glucose, glutamine or amino acids to the fermentor (See column 4, lines 23-26).

In the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to provide the system with individual vessels of glucose, glutamine and amino acids for the known and expected results of providing a means recognized in the art for allowing the control of the individual components of the medium added to the fermentor vessel.

With respect to claims 25, elements (36) and (46) are pumps.

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With respect to claims 30-35, the reference discloses the use of pumps (30, 36, 46) for controlling the flow of fluid within the culture system.

With respect to claims 36 and 37, the fermentor (18) includes a motor driven mixing paddle (20).

6. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Besnainon et al.(US 5,064,764) in view of Tolbert et al. (US 4,537,860) taken further in view of Klebe et al.(US 5,565,353).

The combination of the references of Besnainon et al. and Tolbert et al. has been discussed above.

Claim 24 differs by reciting that the solid support is a culture flask.

The reference of Klebe et al. discloses that it is known in the art to culture adherent cells within a culture flask and that it is known in the art to perfuse a culture flask to replenish the culture medium (See Figure 4).

In view of this teaching, it would have been obvious to employ a culture flask as suggested by the reference of Klebe et al. within the system of the modified primary reference for the known and expected result of providing an alternative bioreactor recognized in the art for allowing cells to be cultured and perfused with a culture medium from an external source as is taught by the primary reference of Besnainon et al.

Terminal Disclaimer

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7. The terminal disclaimer filed on 4/20/07 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent No. 6,696,287 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Response to Arguments

8. With respect to the rejections of the claims under 35 USC 102, Applicants argue (See pages 7-8 of the response filed 4/20/07) that since claim 20 has been incorporated into claim 18, the rejections have been overcome.

In response, the rejections have been withdrawn in view of the amendments to claim 18.

9. With respect to the rejection of claims 20-23 and 28-35 under 35 USC 103 over the reference of Besnainon et al., Applicants argue (See pages 8-9 of the response filed 4/20/07) that the rejection is improper because the bioreactor device of Besnainon et al. does not resemble any of the solid supports required of Applicants' claims.

In response, the instant claims recite that the solid support can be a membrane. The bioreactor of the reference of Besnainon et al. includes membranes. As result, the reference meets the instant claim limitations. Also note, the recited solid support claim language fails to positively recite the solid support as part of the claimed device. The instant claim language merely recites "a culture vessel for growing eukaryotic cells attached to a solid support". The claim never positively recites that the culture vessel includes or comprises a solid support.

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Applicants further comment that one of ordinary skill in the art would not be motivated to employ the solid supports of the instant invention with the device of the primary reference because the claimed supports are not usually rotated.

In response, the Examiner points to page 8, line 4, of the instant specification which states that a roller bottle can be employed as the culture vessel.

Applicants also argue that the vessel of the reference of Besnainon et al. is not considered to be a "tissue culture flask".

In response, the amendments to the claims no longer require that the vessel be a tissue culture flask. See the Examiner's comments concerning claim 24 in the rejection of record. Additionally, the reference of Klebe et al. has been cited to address this claim limitation if it is considered to be positively recited as part of the claimed device.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys J. Corcoran can be reached on 571-272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/William H. Beisner/
Primary Examiner
Art Unit 1744

WHB